On page 2 of the Office Action, the Examiner has objected to the drawings "because of the defects noted on the PTO-948." This objection is noted and will be addressed at a later date upon allowance of the application.

On page 2 of the Office Action, the Examiner levels a rejection under 35 U.S.C. §112, second paragraph, stating that "[t]he term 'glycopeptide' in claim 3 is vague and indefinite. It is not clear what glycopeptide out of myriads of known glycopeptides is encompassed by the claim. The term is not defined either in the art or in the specification." However, the specification (page 4, lines 26-30) defines glycopeptides as "(a group of molecules among which the naturally occurring molecules usually contain a heptapeptide and one or more sugar moieties), whether naturally produced and isolated (such as vancomycin, teicoplanin, etc.) or semisynthetic preparations." Furthermore, the term "glycopeptides" in the context of the present invention is known in the art. Prototype glycopeptides include vancomycin, teicoplanin, ristocetin, avoparcin, A40926, etc. Aglycones derived from these molecules (in which the sugar group is removed chemically or enzymatically) are also included. A review may be found in the volume Glycopeptide Antibiotics, R. Nagarajan (Ed.), Marcel Dekker (1994).

The amendments to the claims to recite that at least one lysostaphin analogue is to be used and that it/they is/are recombinantly produced is supported, for example, by claims 1 and 17 and the specification at page 6, lines 25-27.

Claim 32 is supported by claims 3 and 22.

Claims 33 and 34 are supported at page 10, lines 9-12.

Claim 35 is supported at page 9, lines 30-33, and page 24, lines 21-24.

Claims 36-39 are supported by claim 23 and at page 10, lines 9-12.

Claims 40-43 are supported by claim 24 and at page 10, lines 9-12.

Claims 44-47 are supported by claim 25 and at page 10, lines 9-12.

Claims 48-51 are supported by claim 26 and at page 10, lines 9-12.

Claims 52-55 are supported by claim 27 and at page 10, lines 9-12.

At page 3 of the Office Action, the Examiner has rejected claims 1, 2, 4, 6, 9, 10, 12-16, 19-21 and 23-29 as anticipated under 35 U.S.C. § 102(b) by Zygmunt (Fortschr. Arzneimittelforsch. 16: 309-333, 1972). At page 5 of the Office Action, the Examiner has rejected claims 1, 4, 9, 12-16 and 28-29 as anticipated under 35 U.S.C. § 102(b) by Stark (N.Engl. J. Med. 291: 239-240, 1974). At page 5 of the Office Action, the Examiner has rejected claims 1, 4, 6, 7, 10, 19, 20 and 23-29 as anticipated under 35 U.S.C. § 102(b) by Goldberg (Antimicrob. Ag. Chemother., pp. 45-53, 1967). All pending claims have been limited to methods using or to compositions incorporating recombinantly produced lysostaphin analogue(s). Hence, all anticipation rejections under 35 U.S.C. § 102(b) are mooted as Zygmunt, Stark and Goldberg do not teach recombinantly produced lysostaphin analogue(s).

At page 6 of the Office Action, the Examiner has rejected claims 1, 17, 18, 28 and 31 as obvious under 35 U.S.C. § 103(a) over Oldham (J. Dairy Sci. 74: 4175-4182, 1991) combined with Zygmunt, Stark or Goldberg. This rejection is respectfully traversed. Admittedly, Oldham describes an evaluation of recombinantly produced lysostaphin as a therapeutic. However, the evaluation is limited to the treatment of intramammary staphylococcal infections.

Here, the application and newly amended claims do not speak to a method for treating intramammary staphylococcal infections. Rather, amended claim 4 and its dependent claims speak to a method for treating staphylococcal infections in mammalian heart valve tissue, blood tissue, kidney tissue, lung tissue, bone tissue and meninges tissue. Similarly, amended claim 5 and its dependent claims speak to a method for treating staphylococcal infections associated with a catheter or a prosthetic device but not to the use disclosed by Oldham.

Oldham discusses the use of recombinantly produced lysostaphin only in mammary tissue, and does not discuss its use in other tissue types such as those cited by the pending claims; the context in which lysostaphin is to be used according to the instant invention is not that of the disclosure of Oldham. While Zygmunt, Stark and Goldberg do discuss the use of lysostaphin in contexts other than that of Oldham, they all teach the use of nonrecombinant lysostaphin, and there is no motivation or suggestion to combine any of these references with Oldham. In order to establish a *prima facie* case of obviousness "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." MPEP 706.02(j). Oldham discusses the use of recombinant lysostaphin only in regard to treating intramammary staphylococcal infections, and there is no suggestion or motivation to combine Oldham with Zygmunt, Stark or Goldberg. Accordingly, Applicants respectfully submit that Oldham cannot make up for the deficiencies of the Zygmunt, Stark and Goldberg references to establish a valid basis for an obviousness rejection of the pending claims.

At page 6 of the Office Action, the Examiner has rejected claims 1, 4-6, 28 and 29 as obvious under 35 U.S.C. § 103(a) over Zygmunt, Stark or Goldberg, and further in view of admitted prior art. This rejection is respectfully traversed. The Examiner states on page 7 of the Office Action that "it would be obvious to develop and use new, more potent analogs of [lysostaphin]". However, although the desirability of developing more potent analogs of lysostaphin would be obvious, that does not make the actual conception and development of lysostaphin analogues obvious. Applicants respectfully submit that the Examiner has improperly underestimated the value of the contribution made by the methods and compositions involving potent new analogs taught by their application. Furthermore, the Examiner cites, as proof of the obviousness of developing lysostaphin analogues, Applicants' own disclosure in the instant

application regarding the types of analogues that can be used in the practice of the present invention. Clearly, this is not a valid reason for asserting an obviousness bar to patentability.

At page 7 of the Office Action, the Examiner has rejected claims 2, 3, 21, 22, and 28-30 as obvious under 35 U.S.C. § 103(a) over Zygmunt and further in view of Dixon (Yale J. Biol. Med. 41: 62-68, 1968). This rejection is respectfully traversed. The Examiner states on page 7 of the Office Action that "Zygmunt teaches that a single dose of lysostaphin is effective against staphylococcal infection only for limited time, and it is preferable to follow lysostaphin with another antibiotic. Further, Dixon et al. teach that it is preferable to use lysostaphin in combination with other antimicrobials because a single dose usage of lysostaphin reduces dangers of hypersensitivity reaction." However, Zygmunt and Dixon et al. do not go beyond these simple broad assertions, and such assertions are prophetic at best. In order to establish a *prima facie* case of obviousness "the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP 706.02(j). Certainly, Zygmunt and Dixon et al. do not teach the use of rifamycin or glycopeptides with recombinantly produced lysostaphin, as is claimed by newly added claims 32, 34, 37, 39, 41, 43, 45, 47, 49, 51, 53 and 55. Nor do they teach a composition comprising recombinantly produced lysostaphin in combination with rifamycin or a glycopeptide, as is claimed by newly added claim 35. Again, it is respectfully submitted that the Examiner has underestimated the value of the contribution made by the methods and compositions involving the administration of recombinantly produced lysostaphin in combination with rifamycin or a glycopeptide taught by the instant application.

The Assistant Commissioner is authorized to charge any fee required with this communication to Deposit Account No. 23-1703.

Entry hereof and favorable consideration is respectfully requested.

Dated: December 10, 1999

Respectfully Submitted,

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